United States
Department of
Agriculture

Office of
Agricultural
Biotechnology

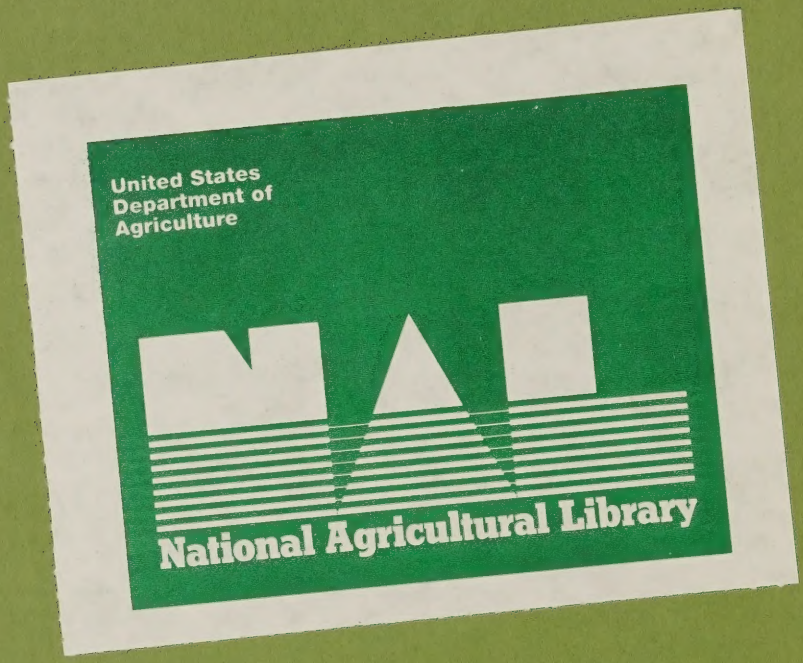
Minutes

Agricultural Biotechnology Research Advisory Committee

Working Group on Biocontainment

August 11-12, 1988

Document No. 88-WG-03



AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE
WORKING GROUP ON BIOCONTAINMENT
U.S. DEPARTMENT OF AGRICULTURE
Room 338-C, Aerospace Building
901 D Street, S.W.
Washington, DC

August 11-12, 1988

The meeting of the Agricultural Biotechnology Research Advisory Committee (ABRAC) Working Group on Biocontainment was called to order on August 11, 1988 at 9:10 a.m., by Dr. Richard Witter, Chair. The meeting was open to the public and was announced in the Federal Register.

Other members of the working group in attendance were Ariel Hollinshead and Nicholas Frey. Fred Gould, Steven Lindow, John Gorham, Peter Carlson and Linda Phaire-Washington were unable to attend. The Office of Agricultural Biotechnology (OAB) was represented by Daniel Jones, Graham Purchase, Philip O'Berry and Eva Russnak. Others present were: Sue Tolin, Chair of the Research Guidelines Working Group; M. S. Barbeito, and Richard Parry, Agricultural Research Service (ARS); Elizabeth Milewski, Environmental Protection Agency (EPA); John Austin and David Giamporcaro, McDermott, Will and Emery; T. L. Medley, Animal and Plant Health Inspection Service (APHIS); John Irwin, National Institutes of Health (NIH); and Kevin Cannon, Monsanto Company.

Dr. Jones of OAB gave a brief report on the meetings of the other two working groups, concerned with research guidelines and definitions, which met July 28-29 and July 28, respectively. Dr. Jones reported that there was some uncertainty in the Definitions group as to how the definitions were going to be used so it decided to go with broad or general definitions with the understanding that these may need to be modified for specific uses related to the guidelines.

Dr. Tolin reported that the Guidelines group discussed the following:

1) A classification of experiments based on the broad definition of biotechnology supplied by the Definitions group.

2) The basic principle the group decided on was to define a set of fundamental principles that would transcend kingdom-specific experiments in organisms and upon which many specific cases could be evaluated.

3) It was generally agreed that a set of fundamental principles that apply to all experiments would be preferable.

4) The Guidelines Group determined that both the process by which the organism is modified and the inherent risk of the non-modified oragnism are important, and an important premise is that the risk should be estimated relative to the risk of a nonmodified organism.

5) Important features of the risk categories are: a) the modification process; b) the organism and its role in nature; c) the modification relative to its likelihood of occurring naturally; and d) the nature of the insertion, i.e., the source and the trait.

6. The Guidelines Group identified the following aspects of confinement other than physical confinement.

a. Biological confinement is extremely important for field release experiments and three aspects that should be considered are environmental, geographic and genetic means of biological containment.

b. The Guidelines Group agreed that the scale of the experiment was important.

7. The Guidelines Group recommended setting up four levels of confinement for potential human health and environmental effects. Levels of confinement should not be based on what agency or authority conducts the review.

8. The approach agreed upon is to follow where the NIH guidelines on containment left off. Confinement levels need to be defined and written up. The plan is to finish writing and turn the material over to OAB within the week.

Dr. Frey said the description of the confinement levels should be brief rather than laying out the laborious details of various ways to achieve biological containment. A series of equivalents should also be established. Organisms containing direct mutations should be in an exempt category.

Dr. Hollinshead said the description should start out with an introductory statement that very little is known about spatial and temporal movement, and that there are not enough models on which to base these guidelines, and that the use of a temporary, evolving format may be necessary.

Dr. Tolin said that where Appendices P and Q of the NIH guidelines left off is where these guidelines should begin. Another aspect that needs to be considered is the conditions that have been imposed by the regulatory agencies and that it is important that these be worked into the guidelines.

Dr. Poe of APHIS reported on the relationship of APHIS regulations to the guidelines. Once APHIS has determined that an organism is a genetically engineered potential pest, then APHIS determines the

conditions under which a permit is issued on a case by case basis. Some APHIS permits have very few conditions associated with them.

Dr. Witter asked if APHIS had defined confinement levels. Dr. Poe replied APHIS had not. APHIS evaluates permit applications on a case by case basis rather than having a set of guidelines. Most permit applicants are quite careful and thoughtful about what they propose to do. Dr. Witter asked how applicants to APHIS describe procedures, processes and safeguards without guidelines as to how to do it. Mr. Medley responded that it is incumbent upon the applicant to tell APHIS what they are going to do and why they are doing it.

Dr. Milewski of EPA reported that EPA coordinates most of its reviews with APHIS. EPA had tried to define containment, found it to be extraordinarily difficult, and was unable to develop a definition for regulatory purposes. Dr. Milewski reported that the EPA Biotechnology Science Advisory Committee (BSAC) considered the competitive ability of a microorganism to be an important feature and the BSAC also developed criteria to consider in terrestrial and aquatic test systems.

Dr. Witter said he presumed that EPA had not found the need at this point for classification of containment levels according to organism risk. Dr. Milewski replied that EPA had not yet had a need for classification of containment levels.

Dr. Hollinshead asked if EPA plans to utilize reviews of Institutional Biosafety Committees (IBC's) in reaching decisions on specific requests for field testing. Dr. Milewski replied that EPA hopes to publish a proposed rule soon that would have a provision for environmental biosafety committees, which could be IBC's so long as they meet the specifications set out by EPA that environmental expertise be represented. Dr. Tolin asked if there was a statement in APHIS' regulations with regard to IBC's. Dr. Poe responded that it was not stated in the rules, but that APHIS may find it appropriate at some time to require that the IBC be involved.

Dr. Witter asked Dr. Purchase to summarize the concept of the handbook for the working group. After Dr. Purchase's presentation, Dr. Witter observed that the "how to" will be covered in the handbook and that general principles would be covered in the guidelines.

Dr. Hollinshead asked why classification of experiments for level of review should be included. Dr. Purchase indicated that if experiments are classified then the level of containment could be linked with the level of review. Dr. Purchase indicated that the guidelines working group thought the level of review and the level of containment should be separate. Dr. Witter said a classification of confinement by itself would not necessarily be useful unless it were linked to the risk of the organism or the level of review. He said he preferred linkage of the confinement level to the risk of organism rather than to level of review. Dr. Witter suggested a statement of

principle in the preamble along the lines that the level of confinement would depend on the properties of the organisms, means of dispersal, and the characteristics of the test site.

There was substantial discussion on the definition of "confinement". Dr. Hollinshead defined confinement as "that which constrains, encloses or limits the scope of spread or survival of organisms or their products." She said she would prefer using the simple English definition rather than to define it in terms of the way it was being used, since the way it is used is implied in the principles. Dr. Tolin asked for clarification on what is meant by "products". Dr. Hollinshead replied that it means both the genes as well as metabolic products.

Dr. Frey presented what he had prepared on confinement principles for biological organisms and gave examples for each category as follows:

> Physical barriers can be used to prevent the spread or survival of organisms outside the experiment area. Physical barriers include border rows, geographical isolation, soil terraces, tillage or other fences.
>
> Biological barriers can be used to prevent spread or survival of organisms outside the experimental area and to prevent the transfer of genetic materials to non-target organisms. Biological barriers include genetic alterations that disable the organism, that produce sterility or that reduce the ability of an organism to survive.
>
> Environmental barriers can be used to prevent the spread or survival of organisms outside the experimental area. Environmental barriers include temperature extremes such as freezing, water limitations, humidity extremes,or light variations such as day lengths which prevent reproduction.
>
> Chemicals can be used to prevent or control spread or survival of organisms outside the experimental area and to prevent transfer of genetic material to non-target organisms. Chemical treatments include herbicides or other toxins to the test organism, pH alterations, osmotic alterations, reproductive control agents and elimination of essential nutrients.
>
> Scale of research outside the laboratory can minimize the potential for undesirable effects to the environment or on public safety. Field tests on less than 10 acres total at one or more sites can be conducted if the product or organism does not fall within the regulatory purview of any federal agency, and if there is no reason to believe the experiment poses a risk to the environment or to public safety.

Dr. Purchase prepared draft descriptions of confinement level one, level three and level four, but he did not have time to work on level two. He defined confinement levels one, three and four as follows:

> Confinement level 1 would be appropriate for organisms with minimal ability to disseminate into and survive in the environment and with minimal potential for detrimental impact on the environment or other organisms.
>
> Confinement level three would be appropriate for organisms that are likely to be readily disseminated into the environment, can establish themselves in the environment and have great potential for severe detrimental impact on the environment or on other organisms.
>
> Confinement level four would be appropriate for organisms that are likely to be readily disseminated into the environment, can establish themselves and are known pathogens, pests or noxious weeds.

Dr. Purchase provided examples under each of the confinement levels, broken down by confinement category, nature of confinement and purpose.

He said the confinement principles, that might be applied singly or in combination, for Level 1, organisms with minimal ability to disseminate, were:

> Physical barriers would be a fence to keep out undesired human intervention; e.g., vandalism; or to keep in large animals; e.g., cattle or pigs. Level 2 under physical barriers would be a dam or berm to hold ethylenes until organisms in the water die naturally.
>
> Chemical would be to disinfect tools and equipment to prevent cultivating and spraying tools and equipment from carrying organisms in and out of the test area.
>
> Biological confinement would be the use of non-competitive organisms in order that organisms will not colonize the environment and survive outside the test site. He said he did not get to environmental and scale.

The confinement principles, that might be applied singly or in combination, for Level 3, organisms that are likely to be readily disseminated, establish themselves and have a potential for severe detrimental effect, are:

> Physical barriers would be fine mesh screen to prevent the ingress or egress of octopods or other animals, e.g., rodents. Level 2 would be a fence and security guard on duty to prevent

human intervention and the ingress or egress of large animals; e.g., deer. A third level would be water runoff collected and heated to kill organisms that escape in a water runoff.

Chemical would be the use of a herbicide after the experiment to kill all susceptible plants which may have undesirable genes or be carriers of undesirable infectious agents. Level 2 would be widespread dissemination of pheromone, with or without poison to disrupt mating and kill arthropods that may invade or may have left the experimental area. Another level would be to sterilize the soil with methyl bromide to destroy residual weed seeds, arthropods, nematodes and microbes.

Biological would be removing pollen; e.g., detassling of corn and castrating or sterilizing animals to prevent the dissemination of undesirable genes through motile gametes by preventing sexual reproduction.

Environmental would be conducting research in northern latitudes; e.g., citrus canker research in Maryland. The purpose is that winter temperatures would kill the organism or the host.

Scale would be confinement of the experiment to a small number of organisms, small volume of culture or small acreage to reduce the severity of detrimental effects should such occur and to facilitate destruction of test organisms should it be necessary.

After reviewing the draft document on confinement principles, Dr. Frey suggested the need for an introductory statement. Dr. Purchase agreed. In his view, the introduction should state that they are general principles and list some of the things to which they may apply. Dr. Witter suggested the addition of a sentence dealing with the spectrum of organisms that are intended to be covered. Dr. Barbeito said that one method of confinement not included was the natural biological decay rate of organisms in the environment. Dr. Purchase said another one that should be included is physical removal of sex organs. Dr. Purchase suggested that the introduction should indicate that the examples are not meant to be exhaustive and all inclusive.

Dr. Tolin said a goal of ABRAC would be to assign particular organisms or experiments to each of the categories or classes of modified organisms and that classification would then be a part of the guidelines for conducting research. Dr. Witter asked if she saw some kind of a classification of organisms being in the guidelines. Dr. Tolin replied that a classification of organisms could be included either in the guidelines or as an appendix to the guidelines. Dr. Tolin said that one premise upon which the guidelines working group based its discussions is that the risk of conducting biotechnology research with a given organism or trait

should be assessed relative to the risk of conducting research with a nonmodified organism or trait. She said if the risk of conducting research with a particular organism or trait is high, then the risk of conducting the biotechnology research with that organism is also high and requires a correspondingly higher level of approval. She said a second basic premise is that the process by which the organism is modified is important in terms of assessing the potential for introducing a risk or an additional risk factor.

Dr. Witter expressed uncertainty as to how confinement level is anticipated to be linked with the review category. Dr. Tolin said the guidelines group worked primarily on setting up the four classes of modified organisms and did some work on confinement categories or risk levels based on survival, modification, dissemination, gene transfer and consequence. She said the guidelines group looked to the confinement group for clarifying the link between confinement level and review category.

Dr. Hollinshead read aloud a draft introductory statement for the confinement section. It was as follows:

> The purpose of this subpart is to outline principles of confinement for usage in the conducting and handling of biotechnology research or aspects thereof as performed outside the laboratory, and to provide a basis for classifying an organism and/or its products in such a manner as to permit appropriate selection of modes of confinement or to define those available thereto. The primary goal is to limit the spread or survival of organisms or their products from the test site in cases where spread or survival may pose environmental or safety risk.

After some discussion, Dr. Frey suggested amending it to say "...to provide a basis to permit appropriate selection of modes of confinement,..." Dr. Witter said the improvements were significant and that it should be a suitable preamble.

Dr. Witter presented the draft material he had prepared. He said that his material was considered to be an either/or option that could deal with the relationship between confinement principles and the characteristics of the organism in a general way. In his view, this approach was preferable to establishing a classification scheme. In his approach there are different levels of confinement and the principal investigator has the responsibility to choose one that is appropriate. He said there was no specific link to level of review and that was intentional. Dr. O'Berry said he favored this approach because it puts the responsibility on the investigator and the IBC to use their good judgment. That is where the bulk of the knowledge of the work to be done resides and that is where the responsibility ought to be. Dr. Frey said he concurred but offered some minor editorial changes.

Dr. Tolin said that paragraph two, which indicates that the less thoroughly an organism is understood, the greater its potential to cause harm, was discussed by the Guidelines Working Group and that they do not agree. She said the Guidelines Group does not think the lack of knowledge about an organism is necessarily indicative of its potential to cause harm. Dr. Witter said that a modicum of knowledge may be needed in order to select the appropriate containment levels and that a lack of knowledge may indicate a conservative approach. Dr. Hollinshead suggested for clarity that it be broken up into two sentences. Dr. Purchase attempted to clarify what was intended in that there were three subordinate things--if an organism is poorly understood, if an organism has a potential to cause harm and if an organism can spread, then a greater level of confinement is needed. Dr. Hollinshead suggested inserting the word "or" to clarify that they are each separate points. Dr. Tolin said that would satisfy her concern on that particular statement. The statement would read:

> In general, the less thoroughly the organism is understood, or the greater its potential to cause harm, or the greater the ease with which it can spread from and survive outside of the test site, then the greater the degree of the confinement that will be required.

Dr. Witter pointed out that the information developed by Dr. Purchase and Dr. O'Berry represented an example of confinement levels linked to organism characteristics. If the group decided to go this way the subject deserved some discussion on where to draw the lines between categories. He indicated there were four confinement levels and the intent was for each to give some general characteristics of the organism for which this would be appropriate and follow each level with examples.

Dr. Frey commented on the lowest level for biological control. He said he felt it was too stringent. He suggested that the description of the lowest level indicate growth in isolation or conduct of an experiment in isolation from sexually compatible organisms rather than specifying organisms that are non-competitive.

Dr. Witter thanked the three members of the working group for their efforts. He also singled out Dr. Purchase for special thanks because he had prepared virtually all of the materials. Dr. Witter also thanked the OAB staff and the other people. He thanked Dr. Poe for his help in providing the APHIS point of view, which was an important contribution to the discussion.

Dr. Witter adjourned the meeting at 12:02 p.m., August 12, 1988.

Eva Russnak

EVA RUSSNAK
Rapporteur

☆U.S. GOVERNMENT PRINTING OFFICE:1988-241-859:80324